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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 12/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/038,192	DELMAS ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9,12-19,22-28,31 and 33-40* is/are pending in the application.

4a) Of the above claim(s) *3-9,12,23,25-28 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,13-19,24 and 33-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The Request for Continued Examination filed September 27, 2004 is acknowledged and has been entered. Currently claims 1, 3-9, 12-19, 22-28, 31, and 33-40 are pending. Claims 3-9, 12 , 22, 23, 25-28 and 31 are withdrawn from consideration.

Claim Objections

1. Claims 18 and 38 are objected to because of the following informalities: Claims 18 and 38 fail to further limit claims 1 and 33 respectively because the recitation "a body fluid" in claims 18 and 38 is the same as the recitation "a biological sample" in claims 1 and 33. Applicant's specification on page 6 discloses that a "biological sample" means a body fluid. Therefore, claims 18 and 33 fail to further limit the parent claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 33-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an increased level of diglycosylated pyridinoline in an individual compared to a reference level of the marker representing the absence of the disease for diagnosing a synovial disease, does not reasonably provide enablement for a decreased level of diglycosylated pyridinoline in an individual compared to a reference level of the marker representing the absence of the disease for diagnosing

synovial disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a method for diagnosing a synovial disease comprising: I) bringing biological sample from an individual into contact, in vitro, with a means for measuring a specific marker for synovial disease, said specific marker being diglycosylated pyridinoline; ii) determining the level of the specific marker; iii) comparing the level of the marker with a reference level of the specific marker representing the absence of the disease, the level of the marker with respect to the reference level indicating the presence of the synovial disease. The specification on page 8, lines 16-28 discloses using reference levels in the diagnostic application for diagnosing a synovial disease.

The working examples and figures are limited to situations showing increased levels of the marker in diseased patients compared to patients lacking the disease. The disclosure does not disclose situations in which a decrease of the marker is indicative of synovial disease.

Further, Blum et al (European Journal of clinical Investigation) (see previous office action for teachings of Blum et al) show increase levels of markers in disease states. Robins et al (see previous office action for teachings of Robins et al) also disclose increased levels of the marker in arthritic disease. However, the prior art does not indicate decreased levels in disease states. At best the diagnoses of synovial disease can only be determined by the indication of increased levels of diglycosylated pyridinoline compared to a reference level of the specific marker representing the absence of the disease. Such is not seen as sufficient to support the breath of the claims and one skilled in the art cannot practice the claimed invention without undue experimentation, because in order to diagnose a synovial disease, one skilled in the art would have to have a high level of predictability, in order to successfully diagnose the synovial disease, and one cannot diagnose synovial disease in which a decreased level of the significant marker is detected without guidance or predictability.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 13-19, 24 and 33-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because monitoring the evolution of a synovial disease implies at least sampling at different time levels and applicant has not positively recited more than one sample from an individual. Therefore, it is unclear how one would determine a progression of the disease without somehow collecting and measuring more than a single sample. Please clarify.

Claim 33 is vague and indefinite because it is unclear if an increase or a decrease in diglycosylated pyridinoline level is indicative for the synovial disease. For example, does a decrease in the level of diglycosylated pyridinoline level in an individual compared to a reference level indicate the individual has the disease? Please clarify. Applicant is cautioned in the event of amendment to the claim not to introduce new matter. Further, in the event of amendment Applicant is required to show support for the amendment in the specification.

Claim 24, line 4 the recitation "mention of a reference level" is vague and indefinite. It is unclear what applicant intends. Is the means for measuring a specific marker labeled with a reference value? Is the mention of a reference included in a set of instructions?

Claim 40, line 3, the recitation "mention of a reference level" is vague and indefinite. It is unclear what applicant intends. Is the means for measuring a specific marker labeled with a reference value? Is the mention of a reference included in a set of instructions?

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 24 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robins et al (WO 89/12824) in view of

Robins et al disclose the measurement of glycosylated pyridinoline. Robins et al disclose the use of antibodies (means for measuring) directed toward the diglycosylated pyridinoline used in immunoassays.

Robins et al differ from the instant invention in failing to teach packaging the components into a kit and also fails to mention a reference.

Foster et al (US 4,444,879) disclose kits containing instructions and controls and standards (Fig. 6 and column 15).

It would have been obvious to one or ordinary skill in the art to package the reagents of Robins et al into a kit and included instructions in the kit as taught by Foster et al because Foster shows reagents and instructions packaged into a kit and one skilled in the art would recognize that the packing of components into test kits makes it more convenient and facile for the test operator.

With respect to the recitation "for synovial disease" as recited in the instant claims. The recitation is directed to the intended use of the reagents and since Robins et al teaches the same reagent for detecting the same specific marker as Applicant and because it would have been obvious to package these components into a kit. Robins et al and Foster et al read on the instantly recited claims. Further, as stated above it is unclear what applicant intends by the recitation " a mention of a reference level.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
November 19, 2004

LONG V. LE
SUPERVISORY PATENT EXAMINER
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11/24/04